AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (original) A gene targeting construct, comprising a transgene encoding a polypeptide comprising a rod outer segment (ROS) targeting signal, said transgene flanked by 5' and 3' DNA sequences which are homologous to the mouse rhodopsin gene, wherein homologous recombination between said construct and a mouse rhodopsin gene results in operable association between said transgene and a rod-specific regulatory sequence.

2. (original) The construct of claim 1, wherein said polypeptide is a G protein-coupled receptor (GPCR).

3. (original) The construct of claim 2, wherein said GPCR is a cannabinoid receptor.

4. (original) The construct of claim 1, wherein said polypeptide is a fusion protein.

5. (original) The construct of claim 1, wherein said ROS targeting signal comprises SEQ ID NO:4.

6. (original) The construct of claim 1, further comprising a positive selection marker.

7. (original) The construct of claim 6, wherein said positive selection marker is a neomycin resistance gene.

8. (original) The construct of claim 6, wherein said positive selection marker is flanked by loxP sites.

9. (original) The construct of claim 1, further comprising a negative selection marker.

10. (original) The construct of claim 9, wherein said negative selection marker is a diphtheria toxin A fragment gene.

11. (original) The construct of claim 1, wherein said rod-specific regulatory sequence comprises a rhodopsin promoter.

12. (original) The construct of claim 1, wherein the 5' flanking DNA sequence comprises a mouse rhodopsin promoter.

13. (original) The construct of claim 1, wherein the 3' flanking sequence comprises a portion of exon 1 of mouse rhodopsin.

14. (original) The construct of claim 1, wherein the 3' flanking sequence comprises exon 2 of mouse rhodopsin.

15. (original) A vector comprising the construct of claim1.

16. (original) A cell comprising the construct of claim1.

17. (original) A mouse cell whose genome comprises:

(a) a functional disruption of one or both endogenous rhodopsin gene alleles, and

(b) a transgene encoding a polypeptide comprising a ROS targeting signal operably associated with a rod-specific regulatory sequence, wherein said polypeptide is not a rhodopsin.

18. (original) The cell of claim 17, wherein said polypeptide is a GPCR.

19. (original) The cell of claim 18, wherein said GPCR is a cannabinoid receptor.

20. (original) The cell of claim 17, wherein said polypeptide is a fusion protein.

21. (original) The cell of claim 17, wherein said ROS targeting signal comprises SEQ ID NO:4.

22. (original) The cell of claim 17, wherein said genome comprises a functional disruption of both endogenous rhodopsin gene alleles.

23. (original) The cell of claim 17, wherein said transgene is inserted into one or both endogenous rhodopsin gene alleles.

24. (original) The cell of claim 17, which is an embryonic stem cell.

25. (original) The cell of claim 17, which is in a mouse.

26. (original) The cell of claim 17, which is isolated from a mouse.

27. (original) The cell of claim 26, which is a rod cell.

28. (cancelled)

29. (cancelled)

30. (original) A mouse whose genome comprises:

(a) a functional disruption of one or both endogenous rhodopsin gene alleles, and

(b) a transgene encoding a polypeptide comprising a ROS targeting signal operably associated with a rod-specific regulatory sequence, wherein said polypeptide is not a rhodopsin.

31. (original) The mouse of claim 30, wherein said polypeptide is a GPCR.

32. (original) The mouse of claim 31, wherein said GPCR is a cannabinoid receptor.

33. (original) The mouse of claim 30, wherein said polypeptide is a fusion protein.

34. (original) The mouse of claim 30, wherein said ROS targeting signal comprises SEQ ID NO:4.

35. (original) The mouse of claim 30, wherein said genome comprises a functional disruption of both endogenous rhodopsin gene alleles.

36. (original) The mouse of claim 30, wherein said transgene is inserted into one or both endogenous rhodopsin gene alleles.

37. (cancelled)

38. (cancelled)

39. (new) A mouse whose genome comprises:

(a) a functional disruption of one or both endogenous rhodopsin gene alleles, and

(b) a transgene encoding a polypeptide comprising a ROS targeting signal operably associated with a rod-specific regulatory sequence, wherein said polypeptide is not a rhodopsin, and wherein sufficient expression results from said transgene to produce an encoded polypeptide.